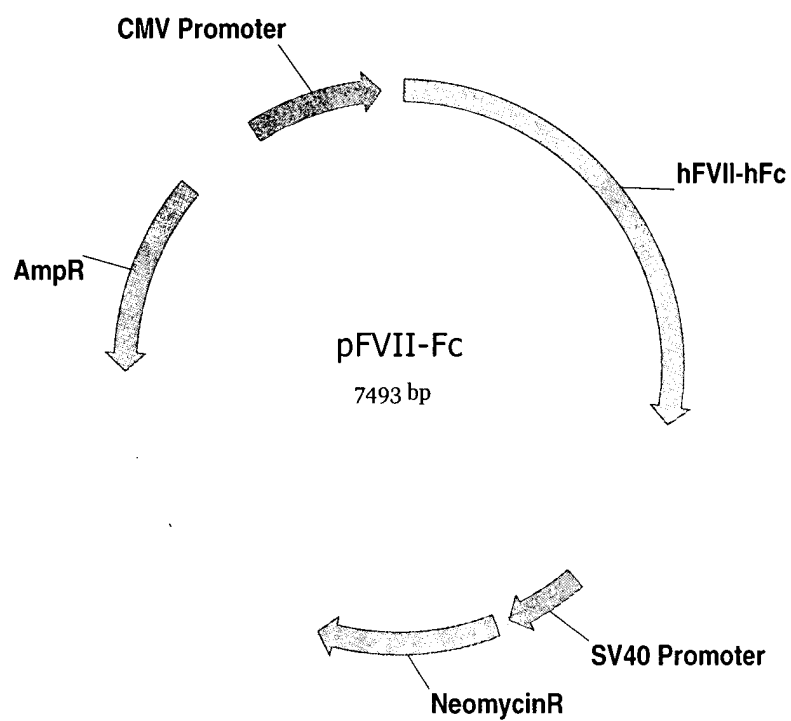


52

1/9

FIGURE 1 – Plasmid vector pFVII-Fc according to example 1

5



53

2/9

FIGURE 2

SEQ ID NO:1 (The amino acid sequence of native human coagulation Factor VII):

5
Ala-Asn-Ala-Phe-Leu-GLA-GLA-Leu-Arg-Pro-Gly-Ser-Leu-GLA-Arg-GLA-Cys-Lys-
5 10 15

GLA-GLA-Gln-Cys-Ser-Phe-GLA-GLA-Ala-Arg-GLA-Ile-Phe-Lys-Asp-Ala-GLA-Arg-
10 20 25 30 35

Thr-Lys-Leu-Phe-Trp-Ile-Ser-Tyr-Ser-Asp-Gly-Asp-Gln-Cys-Ala-Ser-Ser-Pro-
40 45 50

15 Cys-Gln-Asn-Gly-Gly-Ser-Cys-Lys-Asp-Gln-Leu-Gln-Ser-Tyr-Ile-Cys-Phe-Cys-
55 60 65 70

Leu-Pro-Ala-Phe-Glu-Gly-Arg-Asn-Cys-Glu-Thr-His-Lys-Asp-Asp-Gln-Leu-Ile-
75 80 85 90

20 Cys-Val-Asn-Glu-Asn-Gly-Gly-Cys-Glu-Gln-Tyr-Cys-Ser-Asp-His-Thr-Gly-Thr-
95 100 105

Lys-Arg-Ser-Cys-Arg-Cys-His-Glu-Gly-Tyr-Ser-Leu-Leu-Ala-Asp-Gly-Val-Ser-
25 110 115 120 125

Cys-Thr-Pro-Thr-Val-Glu-Tyr-Pro-Cys-Gly-Lys-Ile-Pro-Ile-Leu-Glu-Lys-Arg-
130 135 140

30 Asn-Ala-Ser-Lys-Pro-Gln-Gly-Arg-Ile-Val-Gly-Gly-Lys-Val-Cys-Pro-Lys-Gly-
145 150 155 160

Glu-Cys-Pro-Trp-Gln-Val-Leu-Leu-Leu-Val-Asn-Gly-Ala-Gln-Leu-Cys-Gly-Gly-
165 170 175 180

35 Thr-Leu-Ile-Asn-Thr-Ile-Trp-Val-Val-Ser-Ala-Ala-His-Cys-Phe-Asp-Lys-Ile-
185 190 195

54

3/9

Lys-Asn-Trp-Arg-Asn-Leu-Ile-Ala-Val-Leu-Gly-Glu-His-Asp-Leu-Ser-Glu-His-
200 205 210 215

5 Asp-Gly-Asp-Glu-Gln-Ser-Arg-Arg-Val-Ala-Gln-Val-Ile-Ile-Pro-Ser-Thr-Tyr-
220 225 230

Val-Pro-Gly-Thr-Thr-Asn-His-Asp-Ile-Ala-Leu-Leu-Arg-Leu-His-Gln-Pro-Val-
235 240 245 250

10 Val-Leu-Thr-Asp-His-Val-Val-Pro-Leu-Cys-Leu-Pro-Glu-Arg-Thr-Phe-Ser-Glu-
255 260 265 270

Arg-Thr-Leu-Ala-Phe-Val-Arg-Phe-Ser-Leu-Val-Ser-Gly-Trp-Gly-Gln-Leu-Leu-
15 275 280 285

Asp-Arg-Gly-Ala-Thr-Ala-Leu-Glu-Leu-Met-Val-Leu-Asn-Val-Pro-Arg-Leu-Met-
290 295 300 305 306

20 Thr-Gln-Asp-Cys-Leu-Gln-Gln-Ser-Arg-Lys-Val-Gly-Asp-Ser-Pro-Asn-Ile-Thr-
310 315 320

Glu-Tyr-Met-Phe-Cys-Ala-Gly-Tyr-Ser-Asp-Gly-Ser-Lys-Asp-Ser-Cys-Lys-Gly-
325 330 335 340

25 Asp-Ser-Gly-Gly-Pro-His-Ala-Thr-His-Tyr-Arg-Gly-Thr-Trp-Tyr-Leu-Thr-Gly-
345 350 355 360

Ile-Val-Ser-Trp-Gly-Gln-Gly-Cys-Ala-Thr-Val-Gly-His-Phe-Gly-Val-Tyr-Thr-
30 365 370 375

Arg-Val-Ser-Gln-Tyr-Ile-Glu-Trp-Leu-Gln-Lys-Leu-Met-Arg-Ser-Glu-Pro-Arg-
380 385 390 395

35 Pro-Gly-Val-Leu-Leu-Arg-Ala-Pro-Phe-Pro
400 405 406

55

4/9

SEQ ID NO:2 (DNA primer 1 for preparation of hFVII-hFc):

5'- GCTAGCCACCATGGTCTCCCAGGCCCTCAG -3' (SEQ ID NO:2)

5 SEQ ID NO:3 (DNA primer 2 for preparation of hFVII-hFc):

5'- CGAGCCCCATTTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:3)

SEQ ID NO:4 (DNA primer 3 for preparation of hFVII-hFc):

5'- CGAGCCCCATTTCCCGGATCCGCAGAGCCCAAATCTTGT -3' (SEQ ID NO:4)

10

SEQ ID NO:5 (DNA primer 4 for preparation of hFVII-hFc):

5'- TTGCCGGCCGTCGCACTCATTTA -3' (SEQ ID NO:5)

15 SEQ ID NO:6 (The amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. :

MVSQALRLLCLLLGLQGCLAAGGVAKASGGETRDMPWKPGPHRVFTQEEAHGVLHRRRRANAF
LEELRPGSLERECKEEQCSFEEAREIFKDAERTKLFWISYSDGDQCASSPCQNGGCKDQLQSYICF
20 CLPAFEGRNCETHKDDQLICVNENGGCEQYCS DHTGTRSCRCHEGYSLLADGV SCTPTVEYPCGKI
PILEKRNASKPQGRIVGGKVC PKGEC PWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWRNLIA
VLGEHDLSEHDGDEQSRRVAQVIIPSTYVPGTTNHDIALRLHQPVVLTDHVVPLCLPERTFSERTLAF
VRFSLVSGWGQLDRGATALELMVLNVPRMTQDCLQQSRKVG DSPNITEYMFCAGYSDGSKDSCK
GDSGGPHATHYRG TWYLTGIVSWGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLRAPFP
25 GSAEPKCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYV
DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREP
QVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDK
SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

30

SEQ ID NO:7 (Amino acid sequence of Fc domain from IgG1):

EPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV
EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY
35

TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKLTVDKSR
WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

5

SEQ ID NO:8 (The amino acid sequence of native human coagulation Factor VII conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined, X refers to GLA residues):

10 ANAFLLXLRPGSLXRXCKXXQCSFXXARXIFKDAXRTKLFWISYSDGDQCASSPCQNGGSCCKDQLQS
YICFCLPAFEGRNCETHKDDQLICVNEGGCEQYCSDHTGTRSCRCHEGYSLLADGVSCTPTVEYP
CGKIPILEKRNASKPQGRIVGGKVCPKGECPWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWR
NLIAVLGEHDLSEHDGDEQSRRVAQVIIPSTYVPGTTNHDIALRLHQPVVLTDHVVPLCLPERTFSE
RTLAFVRFSLVSGWGQLLDRGATALELMVLNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDGSK
15 DSCKGDSGGPHATHYRGTWYLTGIVSWGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLR
APFPGSAEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPEVKFN
WYVDGVEVHNAKTKPREEQYNSTYRVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPVLDSGDSFFLYSKL
VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

20

SEQ ID NO:9 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1:

atggtctcccaggccctcaggctcctctgccttctgcttgggcttcagggtgcctggctcaggcgggctcgctaaggcctcaggaggagaaa
cacgggacatgcccgtggaagccggggcctcacagagcttctgtaaccaggaggaagcccacggcgtcctgcacccggcgccggcgccg
25 aacgggttcttgaggagctgcggccgggtccctggagaggagtgcaaggaggagcagtgctccttcgaggaggcccgaggatcttc
aaggacgcggagaggacgaagctgttctggaattcttacagtgatggggaccagtgctcctcaagtccatgccagaatgggggctcctgcaag
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30 ggtgtcctgcacaccacagttgaatatccatgtggaaaaatacctattctagaaaaaagaaatgccagcaaaccccaaggcgaattgtg
ggggcaagggtgtcccaaaaggggagtgatgcagggtcctgtgtgtggaatggagctcagttgtgtggggggaccctgatcaacacca
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aacaactacaagaccacgctcccgtgctggactccgagcgtccttctctacagcaagctaccgtggacaagagcaggtggcagca
ggggaacgtcttctcatgctccgtgatgcatgaggctcgcacaaccactacacgcagaagagccttcccgtctccgggttaaata

5

SEQ ID NO:10 (cDNA sequence encoding the vector comprising the cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with alternative spliced propeptide conjugated to Fc domain of IgG1:

gctagccaccatggtctcccaggccctcaggctcctctgcttctggttccagggtcctggctgcaggcggggtcgctaaggcctcag
10 gaggagaaacacgggacatgccgtggaagccggggcctcacagagctctcgttaaccacaggaggaagcccacggcgtcctgcacggcg
ccggcgcgccaacgcgttcttgaggagctgcggccgggctccctggagaggagtgcaaggaggagcagtgctccttcaggaggccc
gggagacttcaaggacgggagaggacgaagctgttctgatttctacagtatggggaccagtgctcctcaagtcacgagaatgggg
gctctgcaaggaccagctccagtcctatactgcttctgctcctcctgcttccaggggccgaactgtgagacgcacaaggatgaccagctgat
15 ctgtgtgaacgagaacggcggtgtgagcagtagctgacgtgaccacacgggcaccaagcgctcctgtcgggtgccacgaggggtactctctgc
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attaagcggcggggtgtgtgtgtacgcgcagcgtgaccgtacactgccagcgccttagcggccgctccttctccttctccttctcgt
ccacgttgcgggcttccccgtcaagcttaaatcggggctccctttaggttccgatttagtcttacggcaccctgcacccccaaaaactga
ttaggtgatgtttagcagtagtgggcatcgccctgatagacggttttccgctttagcgttggagtcacgttcttaatagtgactctgttccaa
actggaacaacactcaaccctatctcggtctattctttagttataagggatttgcgatttccgctattggttaaaaaatgagctgatttaacaaa
40 aatttaacgcgaattaattctgtggaatgtgtgtagttaggtgtggaagtcccaggtcccagcaggcagaagtagcaaaagcatgcat
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7/9

5 tgtataccgtcgacctctagctagagcttggcgtaatacatggtcatagctgttctgtgtgaaattgttatccgctcacaattccacacacatacga
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 tccgctccatccagctatataattgttccgggaagctagagtaagtagttcgccagttaatagtttgcgcaacggttgcctattgctacaggcat
 25 cgtggtgtcagctcgtcgttggatggtcattcagctccgggtcccaacgatcaaggcgagttacatgatccccatgttgcgaaaaaagcg
 gttagctccttcggtcctccgatcgttgicagaagtaagttggccgcagtggtatcactcatggttatggcagcactgcataattcttactgtcatgc
 catccgtaagatgctttctgtgactggtgagtaactcaaccaagtcattctgagaatagtgatgcggcgacccagttgctctgccggcgctcaat
 acgggataataaccgcgccacatagcagaactttaaaagtgtcatcattggaaaaacgttctcggggcgaaaaactcgaagatcttaccgctg
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 ctcatgagcgggatacatattgaaatgatttagaaaaataaacaataaggggttccgcgcacatttcccgaaaaagtgccacctgacgtcgacg
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 tgcgctgcttcgcatgtacgggacagataacgcttgacattgattgactagttataatagtaataacgaggggtcattagttcatagccc
 35 atatatggagttccggttacataactacggtaaatggccgcctggctgaccgccaacgacccccgccattgacgtcaataatgacgtat
 gtccaagtacgccccctattgacgtcaatgacggtaaatggccgcctggcattatgccagtagcatgacctatgggacttctcacttggcagt
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 ctccacccattgacgtcaatgggagttgtttggcaccaaaaacacgggacttccaaaatgtcgtaacaactccgccccattgacgcaaat
 gggcggtaggcgtgtacggtgggagcttatataagcagagctcttggttaactagagaacccactgcttactggcttatcgaaattaatcgc
 40 actcactatagggagaccaagctg

SEQ ID NO:11 (The amino acid sequence of native human coagulation Factor VII with propeptide (underlined) conjugated to Fc domain of IgG1, native human coagulation Factor VII underlined. Construct is made according to example 1):

40 MVSQALRLCLLLGLQGCLAAVFVTQEEAHGVLHRRRRANAFLEELRPGSLERECKEEQCSFEEAR
EIFKDAERTKLFWISYSDGDQCASSPCQNGGCKDQLQSYICFLPAFEGRNCETHKDDQLICVNN
GGCEQYCSDHTGTRKSCRCHEGYSLLADGVSCTPTVEYPCGKIPILEKRNASKPQGRIVGGKVCPKG
ECPWQVLLLVNGAQLCGGTLINTIWVVSAAHCFDKIKNWRNLIAVLGEHDLSEHDGDEQSRRVAQVII
 45 PSTYVPGTTNHDIALLRLHQPVVLTDHVVPLCLPERTFSERTLAFVRFSLVSGWGQLLDRGATALELM
VLNVPRLMTQDCLQQSRKVGDSPNITEYMFCAGYSDSGSDKDSCKGDSGGPHATHYRGTWYLTGIVS
WGQGCATVGHFGVYTRVSQYIEWLQKLMRSEPRPGVLLRAPFPGSAEPKSCDKTHTCPPCPAPELL
GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRV
VSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVK
 50 GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHY
TQKSLSLSPGK

SEQ ID NO:12 (cDNA sequence encoding the amino acid sequence of native human coagulation Factor VII with propeptide conjugated to Fc domain of IgG1, cDNA construct is made according to example 1):

atggctcccaggccctcaggctcctctgcttctgcttgggttcagggtgcttgcagctctcgttaaccaggaggaagcccacggcgtc
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25

SEQ ID NO:13 (cDNA sequence encoding the vector comprising the cDNA sequence encod-
 ing the amino acid sequence of native human coagulation Factor VII with propeptide conju-
 gated to Fc domain of IgG1, cDNA construct is made according to example 1):

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